Biophytis

LIVE HEALTHIER LONGER

Optimising Obesity Clinical Trials: From Site Selection to Patient Reach

BIO101 + GLP-1RA to prevent muscle loss in patients with overweight and obesity: the OBA study

Waly Dioh PhD MBA
Chief Clinical Operation Officer

Rob van Maanen MD MBA
Chief Medical Officer

Forward Looking Statements

This presentation contains forward-looking statements. Forward-looking statements include all statements that are not historical facts. In some cases, you can identify these forward-looking statements by the use of words such as **«outlook », «believes», «expects», «potential», «continues», «may», «will», «should», «could», «seeks», «predicts», «intends», «trends», «plans», «estimates», «anticipates» or the negative version of these words or other comparable words.** These forward-looking statements include statements regarding Biophytis' anticipated timing for its various BIO101 (20-hydroxyecdysone) clinical trials and expectations regarding commercialization. Such forward-looking statements are based on assumptions that Biophytis considers to be reasonable.

However, there can be no assurance that the statements contained in such forward-looking statements will be verified, which are subject to various risks and uncertainties including, without limitation, delays in patient recruitment or retention, interruptions in sourcing or supply chain, its ability to obtain the necessary regulatory authorizations, COVID-19-related delays, and the impact of the current pandemic on the Company's clinical trials. The forward-looking statements contained in this presentation are also subject to risks not yet known to Biophytis or not currently considered material by Biophytis.

Accordingly, there are or will be important factors that could cause actual outcomes or results to differ materially from those indicated in these statements. Please refer to the «Risk Factors» section of the Company's 2023 Full Year Financial Report available on BIOPHYTIS website *(www.biophytis.com)* and to the risks discussed in the Company's registration statement on Form F-1 and other reports filed with the Securities and Exchange Commission (the "SEC"). We undertake no obligation to publicly update or review any forward-looking statement, whether as a result of new information, future developments or otherwise, except as required by law.

Agenda

1. About Biophytis
2. Medical need for muscle preservation during GLP-1RA treatment for obesity
3. OBA Trial design
4. Main OBA study feasibility drivers

biophytis

LIVE HEALTHIER LONGER

A clinical-stage biotechnology company specialized in the development of therapeutics for muscular and metabolic diseases

HQ location: Paris, France
Other locations in Sao Paulo, BR and Cambridge, MA US

Founded:
2006

Euronext growth Paris (ALBPS)
OTC Market NYC (BPTSY)

Drug discovery : biology of aging for developing drugs for age-related diseases

Multiple partnerships

Academical partnerships

SCIENCES SORBONNE UNIVERSITÉ
MÉDECINE SORBONNE UNIVERSITÉ
INSTITUT DE MYOLOGIE INNOVER POUR GUERIR
INSTITUT DE LA VISION
cnrs
Inserm

Industrial partnerships

Skyepharma
eurofins
SEQENS

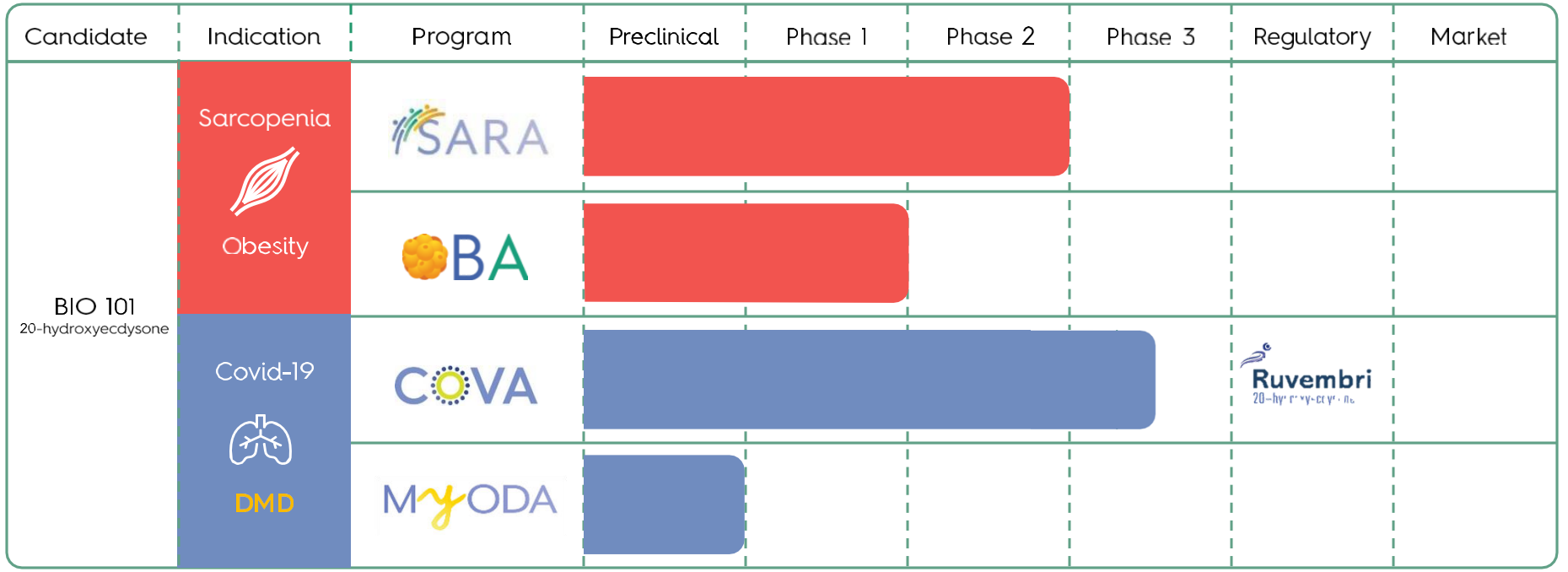
PAGs partnerships

AFM TELETHON

Pharmaceutical partnership

BLANVER

Our Clinical Pipeline as of today



xxx orphan diseases

Agenda

1. About Biophytis
2. Medical need for muscle preservation during GLP-1RA treatment for obesity
3. OBA Trial design
4. Main OBA study feasibility drivers

Loss of Lean Body Mass significant with GLP-1 RA Therapy

GLP-1 RAs are highly effective in weight loss & experiencing rapid uptake

But **25% - 40% of total body weight loss mediated by GLP-1 RA therapy may be attributed to loss of lean mass** [1-3]

Preserving lean muscle mass is important to promote long-term metabolic benefits, sustainable weight management and health outcomes [4-7]

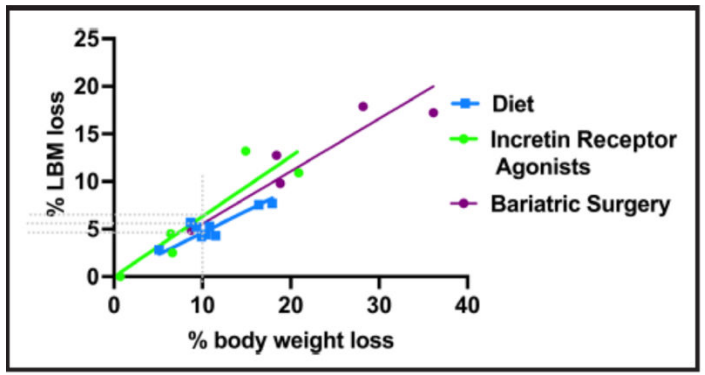
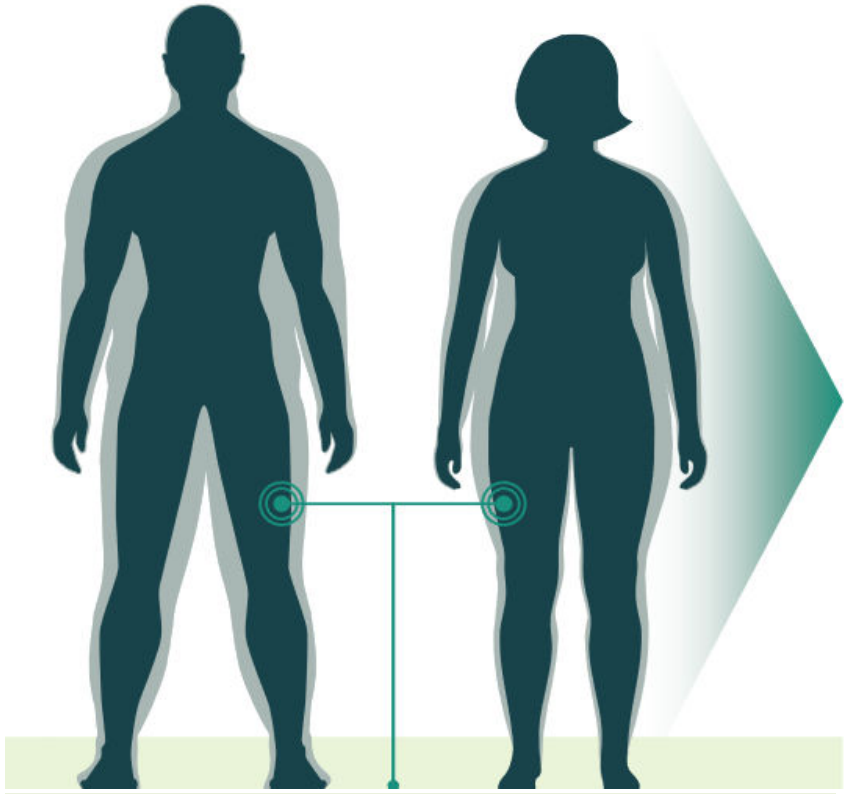


Figure 1. The relationship of percent weight loss to percent loss of lean body mass resulting from dietary intervention, therapy with GLP-1 RA or GLP-1/GIP RA, or bariatric surgery in various studies.[8]



Up to 40% non-fat mass (lean body mass)

Current weight loss strategies challenged by:

- Tolerability
- Lack of durability (rebound)
- Significant lean body mass loss[1-3]

Source : 1. Muller TD, et al Anti-obesity drug discovery: advances and challenges. Nature Reviews Drug Discovery 2022; 21, 201-223;
2. Wilding JPH, Batterham RL, Calanna S, et al. Once-Weekly Semaglutide in Adults with Overweight or Obesity. N Engl J Med. 2021;384(11):989-1002;
3. Jastreboff AM, et al Tirzepatide Once Weekly for the Treatment of Obesity. NEJM 2022; 387 (3): 205-216;
4. Cava et al. Preserving healthy muscle during weight loss. Adv Nutr 2017;8:511-19;
5. Lundgren JR et al. Healthy Weight Loss Maintenance with Exercise, Liraglutide or Both Combined. NEJM 2021;384:1719-30;
6. Beal JW et al. Dietary weight loss-induced improvements in metabolic function are enhanced by exercise in people with obesity and prediabetes. Nat Metab. 2022;5(7):1221-1235;
7. Dulloo AG, et al How dieting makes some fatter: from a perspective of human body composition autoregulation. Proc Nutr Soc. 2012 Aug;71(3):379-89
8. Figure from Linge J et al. Muscle Mass and Glucagon-Like Peptide-1 Receptor Agonists: Adaptive or Maladaptive Response to Weight Loss? Circulation. 2024;150:1288–1298

Agenda

1. About Biophytis
2. Medical need for muscle preservation during GLP-1RA treatment for obesity
3. OBA Trial design
4. Main OBA study feasibility drivers

« It is critical for us to study the safety and efficacy of BIO101 designed to reduce the risk of muscle mass loss »

Pr Cornier, President-elect of Obesity Society

OBA

OBA Phase 2 study: randomized placebo-controlled study in 164 patients with obesity and overweight starting treatment with GLP-1RA

- To evaluate the **efficacy and safety** of 21 weeks of oral 20-Hydroxyecdysone (20E) versus placebo in adult patients starting a GLP-1RA to **reduce the potential muscle strength loss from GLP-1 agonists**

Biophytis

BA

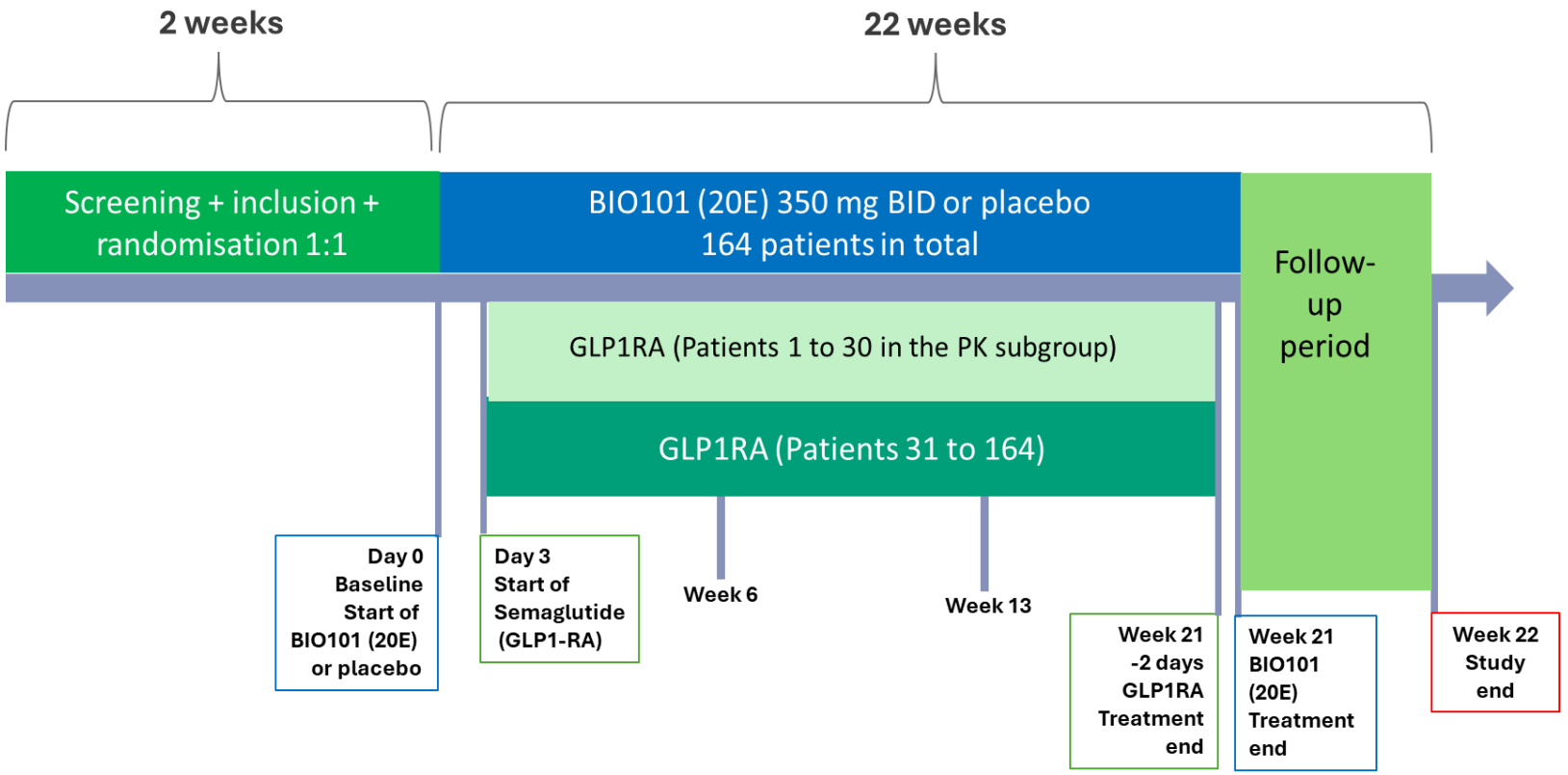
A Phase 2, double-blind, randomized, placebo-controlled multicenter study to evaluate the efficacy and safety of 20-Hydroxyecdysone (20E) in reducing the muscle strength loss from GLP1 agonists in combination with dieting in obese adult patients

Sample size : 164 patients

Target population:

Obese patients BMI ≥30 or overweight (BMI ≥27) with one or more weight-related sequalae (e.g. dysglycemia, hypertension) who will start treatment with semaglutide a GLP-1 agonist.

Site Location :



BA

A Phase 2, double-blind, randomized, placebo-controlled multicenter study to evaluate the efficacy and safety of 20-Hydroxyecdysone (20E) in reducing the muscle strength loss from GLP1 agonists in combination with dieting in obese adult patients

Primary Objective

To assess the efficacy of 20E on muscle strength

Primary Endpoint :

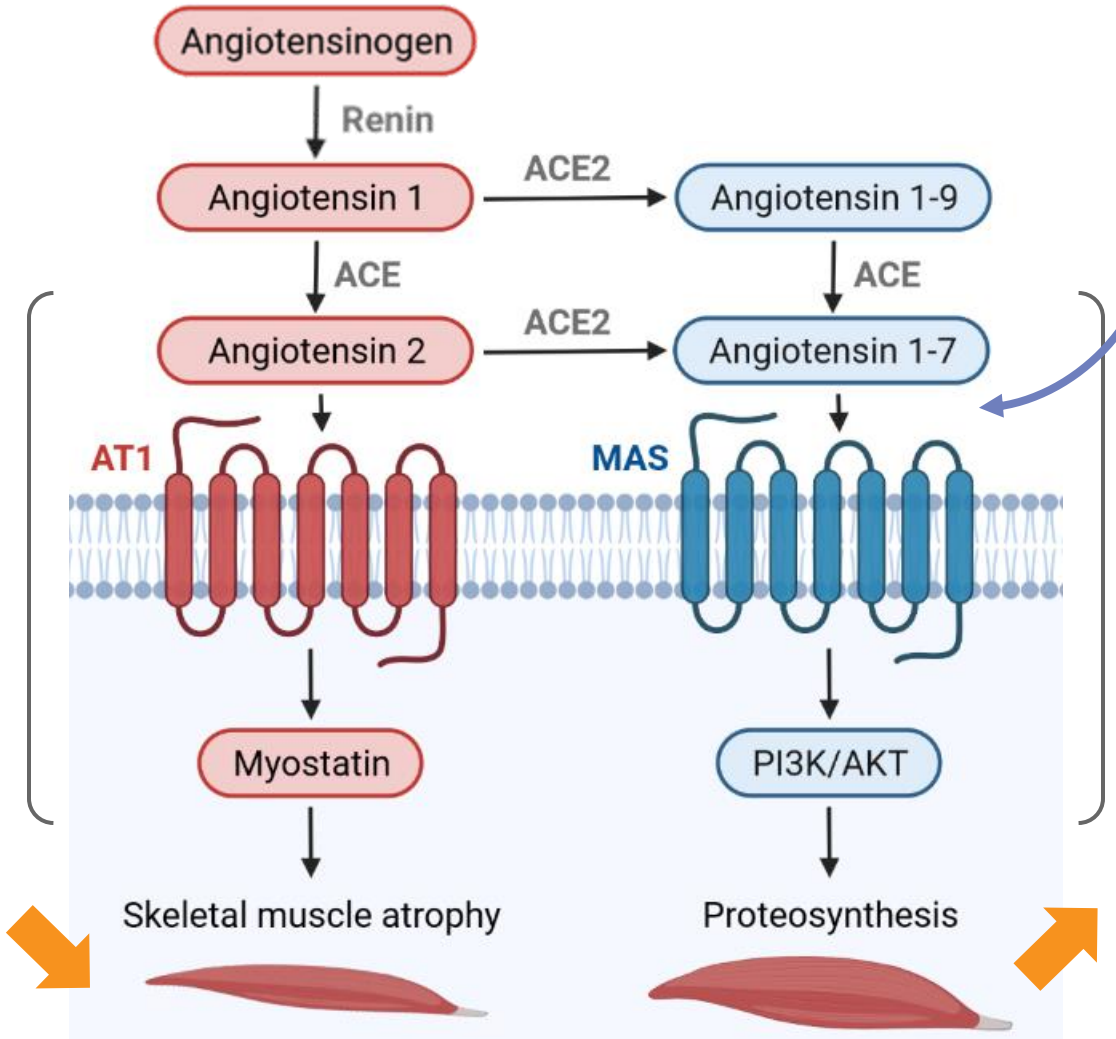
knee extension strength evaluated by isokinetic dynamometry

Secondary and exploratory Objectives

	Endpoints
To explore the efficacy of 20E on another measure of muscle strength	• Knee extension strength at intermediate timepoints • Knee flexion strength evaluated by Isokinetic Dynamometry. • Hand Grip Strength (HGS)
To explore the efficacy of 20E on performance and mobility	• 6MWD • 5XSST • Stair climb
To explore 20E effect on body composition	DXA: appendicular and total lean body mass and fat mass (central reading)
To explore 20E effect on health related QoL	SF-36 WQoL- Lite CT Physical Function score and total score
To explore 20E effect on Body weight and Anthropometry	BMI, Body weight, waist circumference
To explore 20E effect on Insuline sensitivity, glucose control, blood pressure	HOMA, (fasted insulin + glucose) + Hba1c, LDL, HDL, triglycerides Blood pressure: SBP+DBP

Biophytis

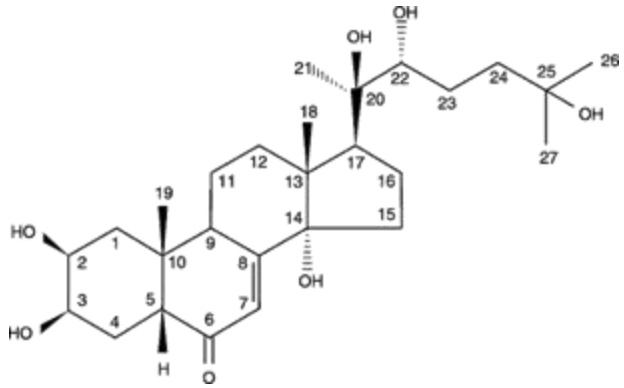
BIO101, a MAS receptor activator with beneficial effect on muscle



Classical arm

Protective arm

BIO101



Ecdysteroides = class of steroid hormones

> J Mol Endocrinol. 2021 Dec 23;68(2):77-87. doi: 10.1530/JME-21-0033.

20–Hydroxyecdysone activates the protective arm of the RAAS via the MAS receptor

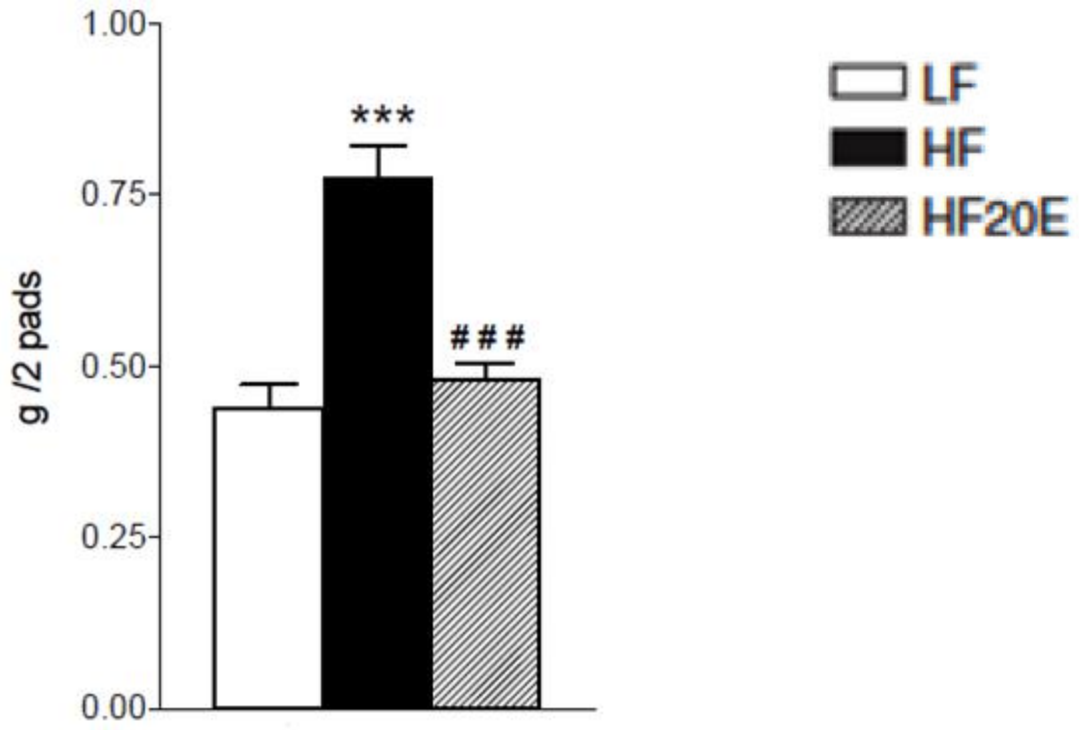
René Lafont [1 2], Maria Serova [1], Blaise Didry-Barca [1], Sophie Raynal [1], Louis Guibout [1], Laurence Dinan [1], Stanislas Veillet [1], Mathilde Latil [1], Waly Dioh [1], Pierre J Dilda [1]

Affiliations + expand

PMID: 34825653 DOI: 10.1530/JME-21-0033

Biophytis

Rationale : previous results in obesity: BIO101 (20E) limits the fat mass development in the high-fat diet mouse model



Epididymal adipose tissue weight

*** $P < 0.001$ vs LF; # # $P < 0.01$ vs HF; # # # $P < 0.001$ vs HF

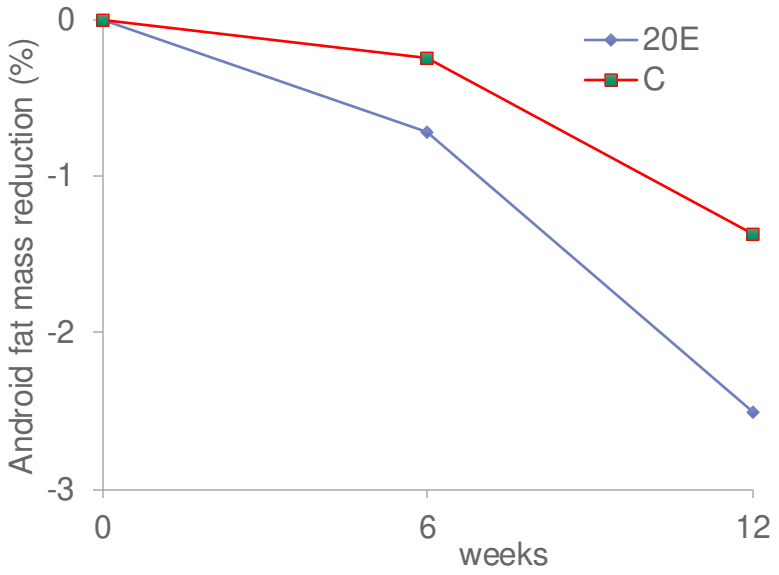
Feeding mice with a high fat (HF) diet:

Addition of 20E (HF20E, 5 mg/kg per day) results in a lower development of adiposity

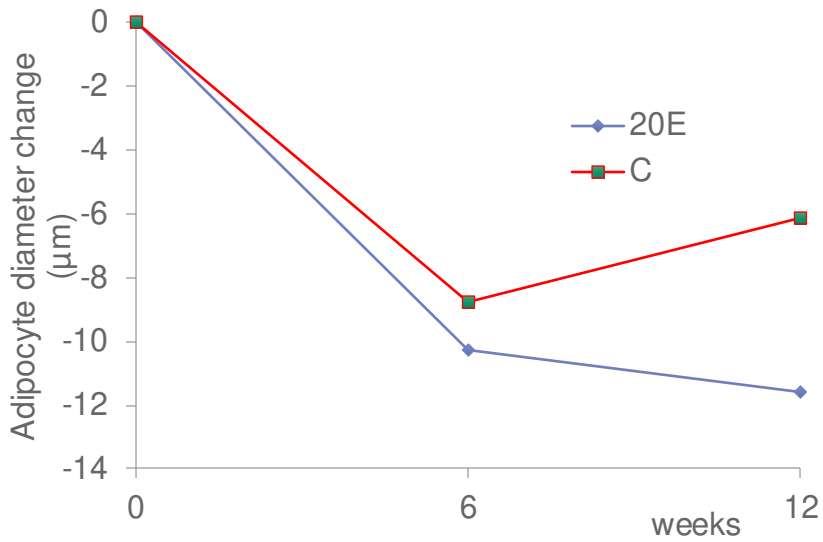
Source : Foucault et al., Obesity 2012

Randomized placebo-controlled study with 37.5 mg 20E in 58 obese and overweight subjects

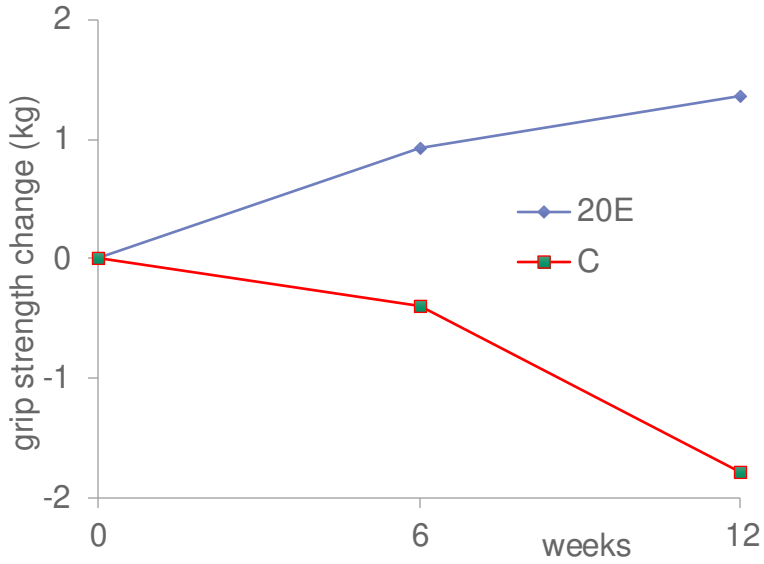
Android fat mass reduction



Adipocyte diameter reduction



Hand grip strength preservation



37.5 mg 20E ■ Placebo ■

Statistically significant decrease of android fat mass (p=0.039)

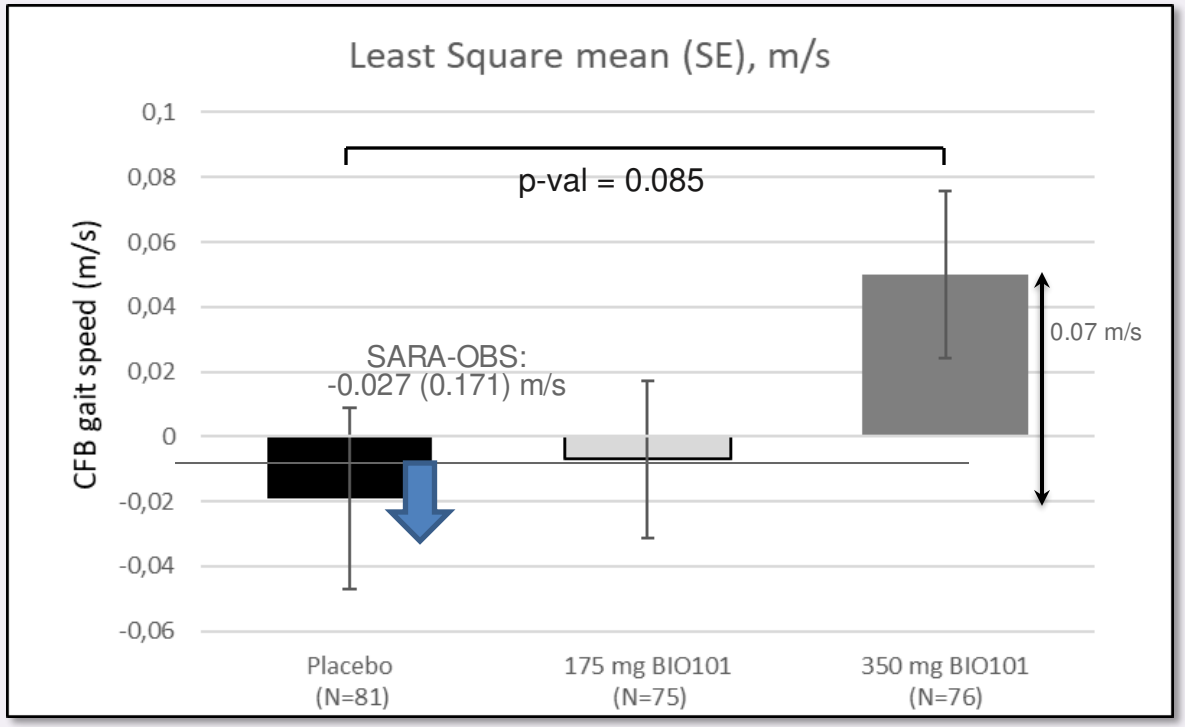
Statistically significant decrease in adipocyte diameter (p=0.032)

Trend for handgrip strenght maintenance in subjects who lost > 5% of their initial weight during the weight loss phase (p=0.097)

Biophytis

Phase 2 SARA-INT : Efficacy analysis overtime *(baseline versus M6)*

Secondary analysis of the primary endpoint: Change from Baseline in Gait speed from 400MWT



FAS Population at M6:
Statistical analysis of Change From Baseline (CFB) in 400MWT gait speed based on Multiple Imputation for subjects without on-site visit data at M6 and adj. Bayesian Imputation for non completers at M6

⇒ Natural deterioration in gait speed in placebo group, similar to the SARA-OBS population

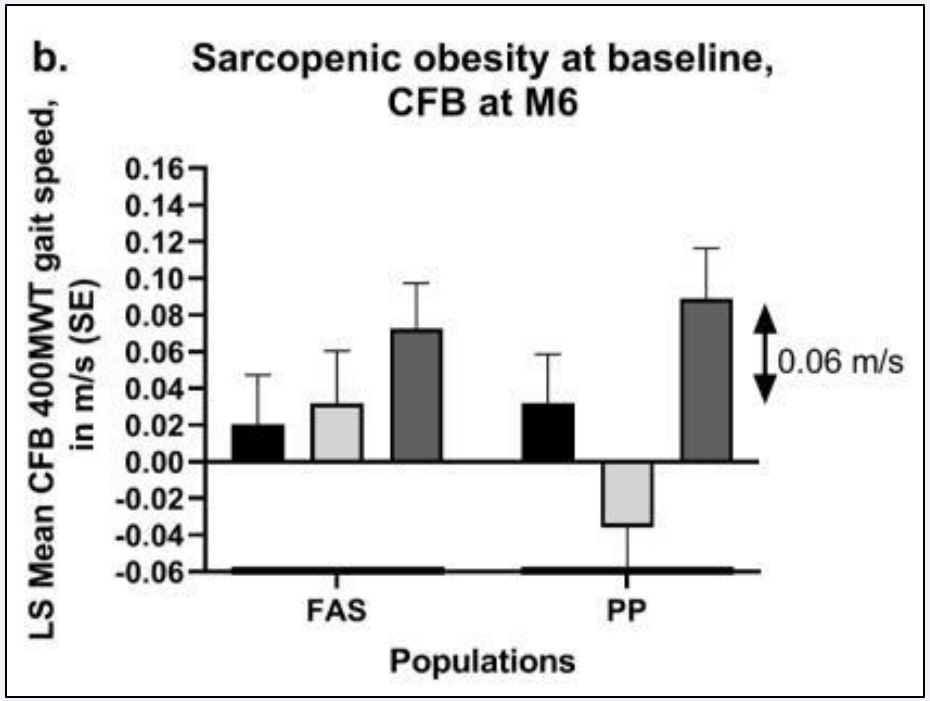
⇒ Close to statistical significance and close to clinical significance at the highest dose

⇒ Trend for a dose effect

Source : CSR SARA INT

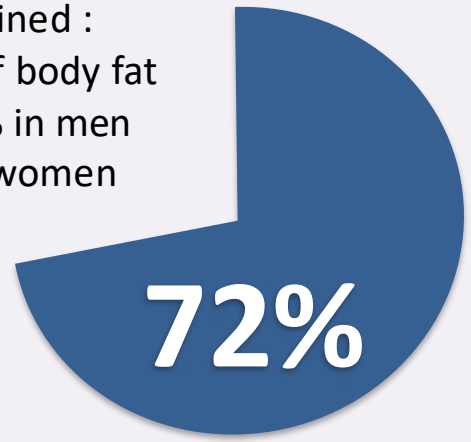
Phase 2 SARA-INT : Efficacy analysis for gait speed from 400MWT

Subgroup analysis in patients with sarcopenic obesity (% of body fat mass of >25% in men and >35% in women)



Placebo
175 mg BID
350 mg BID

Of the 233 randomized were **sarcopenic obese** as defined : percentage of body fat mass of >25% in men and >35% in women



⇒ **Nominally significant treatment effect versus placebo**

Source : CSR SARA INT

Agenda

1. About Biophytis
2. Medical need for muscle preservation during GLP-1RA treatment for obesity
3. OBA Trial design
4. Main OBA study feasibility drivers

OBA Main study feasibility drivers

Main drivers	Activities	Target
Site selection/recruitment strategy	▪ Track record on obesity and physical performance trials ▪ Updated patient database ▪ Sites already involved in previous Biophytis trials ▪ No competition studies ▪ Experienced in Pharmacokinetic studies ▪ Ability to quickly reach a high recruitment rate: eg 5 pts/site/month	• **164 patients with Obesity and overweight** • **6 US sites** • **2 EU sites**
Target population/Patient engagement	▪ Patient Centric Focus ▪ Living in close geographic location ▪ Ensuring diversity ▪ Ensure Patient recruitment, adherence and retention using innovative tools	
Durability and sustained outcomes	▪ Compliance with dieting, protein intake and exercise ▪ Maintain drop out at the lowest rate ▪ Maintain durable weight loss and prevent weight regain ▪ Ensure GLP-1RA availability	
Outsourcing strategy	▪ Ensure an optimized vendor selection process ▪ True collaboration sponsor/vendor from beginning to end ▪ Mid or small size local CROs	

Feasibility Assessments	▪ Body composition measurements:
	  ▪ Fat mass/Fat free mass measurement with DEXA
	▪ Physical performance measurements:
	  ▪ Biodex; Mobility (6MWD; Stair climb etc.…)
	▪ Training the sites and homogenized assessment instructions
	▪ Patient Reported Outcomes (QOL)	

Biophytis

Questions and discussion

Thank you for your attention!

Contact

Waly Dioh waly.dioh@biophytis.com

Rob van Maanen rob.vanmaanen@biophytis.com

Backup

The Need : Optimising the Fat-to-Lean mass ratio associated with AOM

Fat-to-Lean mass ratio

zepbound™ **3,11**

wegovy® **1,98**

Tirzepatide in obese patients was said to be “similar to that reported with lifestyle-based and surgical treatments for obesity,” (Jasteboff et. al. NEJM 2022). In the Ph3 SURMOUNT-1 trial, tirzepatide showed a 3.11-to-1 ratio of fat-to-lean mass loss on a percentage basis (week 72, absolute basis not reported, Jastreboff et. al. NEJM 2022).

Semaglutide at its weight loss dose of 2.4 might have a potentially worse lean mass loss ratio. In the Ph3 trial STEP-1, semaglutide showed less optimal 1.98-to-1 ratio on a percentage basis (1.50-to-1 on an absolute basis, at week 68 Wilding et. al JES 2021 and Wilding et. al. NEJM 2021).

Separately, for patients who stop GLP1+ therapies, it is speculated that they may regain more fat than lean mass in the short term, but it is possible that their bodies may adjust closer to normal over the longer term. Unfortunately, patients’ body composition after stopping therapy remains poorly characterized, and it is unclear which studies (if any) will evaluate this in the future.

Source : Leerink Partners report Biopharma, Feb 11th, 2024

Need : There is a high medical demand for preserving muscle strength

96%

of obese patients have **impaired specific muscle strength** (1)

84%

of obese patients are deemed to have **poor muscle quality** (1)

> In clinical practice, **caregivers should consider strategies to maintain muscle status when applying** surgical or **pharmacological obesity management therapies** (2)
>
> nature International Journal of Obesity

Source : (1) Valenzuela et al. BMC Musculoskeletal Disorders (2020) 21:200, (2) Obesity management strategies should cut fat, not muscle | International Journal of Obesity (nature.com)